

Claims

1. A pharmaceutical composition for stimulating liver regeneration *in vivo*
5 including after chronic/acute liver failure, comprising an effective
amount of a polypeptide comprising an amino acid sequence having
90% amino acid identity with the polypeptide consisting of the amino
acid sequence starting at the amino acid residue 36 and ending at the
amino acid residue 175 of sequence SEQ ID N°1, in combination with
10 at least one physiologically acceptable excipient.
2. A pharmaceutical composition according to claim 1 comprising an
effective amount of the polypeptide consisting of the amino acid
sequence starting at the amino acid residue 36 and ending at the
15 amino acid residue 175 of sequence SEQ ID N°1, in combination with
at least one physiologically acceptable excipient.
3. A pharmaceutical composition according to claim 1 comprising an
effective amount of a polypeptide comprising an amino acid sequence
20 having 90% amino acid identity with the polypeptide consisting of the
amino acid sequence starting at the amino acid residue 27 and
ending at the amino acid residue 175 of sequence SEQ ID N°1, in
combination with at least one physiologically acceptable excipient.
- 25 4. A pharmaceutical composition according to claim 1 comprising an
effective amount of the polypeptide consisting of the amino acid
sequence starting at the amino acid residue 27 and ending at the
amino acid residue 175 of sequence SEQ ID N°1, in combination with
at least one physiologically acceptable excipient.
30
5. A pharmaceutical composition according to claim 1 comprising an
effective amount of the human hepatocarcinoma-intestine-pancreas
/pancreatic-associated protein (HIP/PAP) of sequence SEQ ID N°1 in
combination with at least one physiologically acceptable excipient.
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6. A pharmaceutical composition according to any one of claims 1 to 5, for treating patients having undergone a liver resection.
- 5 7. A pharmaceutical composition according to any one of claims 1 to 5, for treating patients which are the subjects of a partial liver transplant, a hepatic failure caused by liver diseases such as hepatitis, hepatic cirrhosis of alcoholic, viral, drug or unknown cause, or hepatic cancer.
- 10 8. A pharmaceutical composition according to any one of claims 1 to 5, for treating patients which are the subjects of a disease comprised in the group consisting of : Hepatitis B, Hepatitis C, Urea Cycle defects, Familial hypercholesterolemia, Alcohol induced cirrhosis, Glycogen Storage Disease, Autoimmune Hepatitis, Primary Hyperoxaluria type I, Cryptogenic cirrhosis, Crigler-Najjar syndrome type I, Congenital
15 Hepatic Fibrosis, Neimann- Pick Disease, Primary Biliary Cirrhosis, Familial Amyloidosis, Biliary Atresia, Hepatocellular Carcinoma, Primary Sclerosing Cholangitis, Hepatoblastoma, Alagille Syndrome, Hemangioendothelioma, Familial Cholestasis, Non-Carcinoid neuro-endocrine, Drug Induced liver failure, benign liver tumor such as focal
20 nodular hyperplasia Liver tumors such as Hepatocellular carcinoma and Cholangiocarcinoma, Acute/fulminant liver failure, Budd-Chiari syndrome, Alpha-1-antitrypsin deficiency, Wilson Disease, Hemochromatosis, Tyrosinemia, Protoporphyrria, and Cystic fibrosis.
- 25 9. A pharmaceutical composition with limited adverse effects on liver necrosis comprising :
 - (i) a therapeutically effective amount of a hepatotoxic compound, and
 - (ii) an effective amount of a polypeptide according to anyone of
30 claims 1 to 5.
10. A composition comprising dividing hepatocytes in combination with a polypeptide according to anyone of claims 1 to 5.
- 35 11. A composition comprising hepatocytes that have been transfected with an expression cassette that drives the expression of a

polypeptide according to anyone of claims 1 to 5 in said transfected hepatocytes.

5 12. A composition comprising an effective amount of bone-marrow stem cells in combination with a polypeptide according to anyone of claims 1 to 5.

10 13. A pharmaceutical composition for stimulating liver regeneration *in vivo* comprising an effective amount of a composition according to anyone of claims 10 to 12.

14. A process for stimulating hepatocyte growth *in vitro* comprising :
 (a) collecting hepatocytes;
 (b) cultivating said hepatocytes in an appropriate culture medium ;
15 and
 (c) treating said hepatocytes with a mitogenic amount of a polypeptide according to anyone of claims 1 to 5.

20 15. A process for stimulating hepatocyte growth *in vitro* comprising :
 (a) collecting hepatocytes;
 (b) cultivating said hepatocytes in an appropriate culture medium ;
 and
 (c) transfecting said hepatocytes with an expression cassette that drives the expression of the HIP/PAP protein in said transfected
25 hepatocytes.

16. A process for treating bone marrow stem cells *in vitro* comprising :
 (a) collecting bone marrow stem cells;
 (b) cultivating said bone marrow stem cells in an appropriate culture
30 medium ; and
 (c) treating said bone marrow stem cells with a mitogenic amount of a polypeptide according to anyone of claims 1 to 5.

17. Use of a polypeptide according to anyone of claim 1 to 5, to manufacture a pharmaceutical composition for stimulating liver regeneration *in vivo*.

AMENDED CLAIMS